

Remarks/Arguments

A. Pending Claims

Claims 1, 9-10, 13-15, and 19-21 are currently pending. Claims 1, 5, and 21 have been amended. Claims 22-36 have been cancelled without prejudice.

B. The Claims Are Not Indefinite Pursuant To 35 U.S.C. § 112, First Paragraph

Claims 1, 5, 9-11, 13, 14, and 19-36 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicant respectfully disagrees with this rejection; however, to expedite the case Applicant has amended the claims for clarification.

C. The Claims Are Patentable Over Supersaxo In View Of Rembaum Pursuant to 35 U.S.C. §103(a)

The Examiner rejected claims 1, 5, 9, 13-15, 19-29, 31, 32 and 34-36 under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,470,582 to Supersaxo et al. (hereinafter “Supersaxo”) in view of U.S. Patent No. 4,406,750 to Rembaum (hereinafter “Rembaum”). Applicant respectfully disagrees that the claims are unpatentable over Supersaxo in view of Rembaum.

To establish a *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); MPEP 2143.03.

Amended claim 1 states:

preparing biodegradable porous microspheres comprising cationic functional groups from a mixture of a biocompatible material comprising cationic functional groups and a biodegradable polymer;

adding a solution comprising a biopharmaceutical compound to the biodegradable porous microspheres;

incorporating the biopharmaceutical compound into the biodegradable porous microspheres through ionic interaction by suspending or equilibrating the biodegradable porous microspheres in a solution comprising the biopharmaceutical compound at a pH beyond the pI of the biopharmaceutical compound; and

recovering and freeze-drying the biopharmaceutical-incorporated microspheres;

Amended Claim 21 states:

a biodegradable porous microsphere, comprising cationic functional groups from a mixture of a biocompatible material comprising cationic functional groups and a biodegradable polymer; and

a biopharmaceutical compound, wherein the biopharmaceutical compound is incorporated into the biodegradable porous microspheres through ionic interactions.

The Office Action states that, “Supersaxo et al. discloses a controlled release pharmaceutical composition comprising a physiologically active agent dispersed in preformed porous polymeric microparticles.” (Office Action, page 4) The Examiner concedes that “Supersaxo does not disclose the microparticles having accessible ionic functional groups.”

To remedy the deficiencies of Supersaxo, the Office Action relies on the teachings of Rembaum. Specifically, the Office Action states that “it would have been obvious for one of ordinary skill in the art at the time of the instant invention to add polymers or polymeric segments carrying cationic groups such as quaternary groups ... to the biocompatible or biodegradable polymers of Supersaxo so as to functionalized or add functionalized groups to the polymers....” Applicant respectfully disagrees with the Examiner’s assertion of obviousness.

Claims 1 and 21 include a combination of features including, but not limited to, the features of “preparing biodegradable porous microspheres comprising cationic functional groups.” Applicant submits that the cited art does not appear to teach or suggest at least the quoted features of claims 1 and 21. Applicant submits that biodegradable porous microspheres are microspheres that will degrade over time in the body. Supersaxo appears to teach the use of biodegradable polymers. Rembaum, however, does not appear to teach or suggest the use of biodegradable polymers. Specifically, Rembaum is directed to the formation of polyacrylate polymers. For example, Rembaum states:

The beads are prepared by the aqueous suspension polymerization of a monosaturated, bromo, chloro, iodo, or tertiary amine substituted acrylic monomer and 0.1 to 30% by weight of a cross-linking agent.
(Rembaum, col. 3, lines 32-35)

The cross-linked porous beads are insoluble and swellable in water and are insoluble in common inorganic and organic solvents.
(Rembaum, col. 5, lines 29-32)

Applicant submits that the monomers of Rembaum do not appear to produce a biodegradable polymer. Applicant further submits that adding the monomers of Rembaum to the monomers of Supersaxo would not appear to produce a biodegradable polymer. As such, Applicant submits that the Office Action does not provide sufficient support for the assertion that the combination of Supersaxo and Rembaum would render obvious the features of Applicant’s claims. Adding a monomer that produces a polymer that is not biodegradable to a monomer that produces a biodegradable polymer would not be an obvious procedure if the desired result is to produce a biodegradable polymer. An obvious rejection based upon a modification of a reference that destroys the intent, purpose or function of the invention disclosed in the reference, is not proper and the case of obviousness cannot be properly made. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Additionally, Applicant’s claims are directed to a sustained release pharmaceutical composition. Rembaum teaches, in the case of polyanions such as heparin, DNA, RNA and bile acids, that

irreversible binding may be formed. Rembaum does not appear to teach or describe the binding of peptides or proteins. Rembaum does appear to teach that reversible binding to monoanions having a low molecular weight, such as penicillin, pesticides, sex attractants, etc may be formed and thus used in a slow release formulation. Therefore, it would appear that for polyanions, such as peptides and proteins would bind to the polymers of Rembaum irreversibly. The combination of irreversible binding and non-degradable polymers would not be suited for a sustained release composition.

Applicant submits that the cited art does not appear to teach or suggest, alone or in combination, the features of claims 1 and 21. Applicant respectfully requests removal of the rejection to claims 1 and 21 and the claims dependent thereon.

D. The Claims Are Patentable Over Supersaxo In View Of Schwendeman Pursuant to 35 U.S.C. §103(a)

The Examiner rejected claims 1, 5, 9, 13-15, 19-29, 31, 32 and 34-36 under 35 U.S.C. § 103(a) as obvious over Supersaxo in view of U.S. Patent No. 6,326,021 to Schwendeman et al. (hereinafter “Schwendeman”). Applicant respectfully disagrees that the claims are unpatentable over Supersaxo in view of Schwendeman.

The Office Action states that, “Supersaxo et al. discloses a controlled release pharmaceutical composition comprising a physiologically active agent dispersed in preformed porous polymeric microparticles.” (Office Action, page 4) The Examiner concedes that “Supersaxo does not disclose the microparticles having accessible ionic functional groups.”

To remedy the deficiencies of Supersaxo, the Office Action relies on the teachings of Schwendeman. Specifically, the Office Action states that “it would have been obvious for one of ordinary skill in the art at the time of the instant invention to add polymers or polymeric segments carrying cationic groups such as amines ... to the biocompatible or biodegradable

polymers of Supersaxo so as to functionalized or add functionalized groups to the polymers....”

Applicant respectfully disagrees with the Examiner’s assertion of obviousness.

Claims 1 and 21 include a combination of features including, but not limited to, the features of “incorporating the biopharmaceutical compound into the biodegradable porous microspheres through ionic interaction.” Applicant submits that the cited art does not appear to teach or suggest at least the quoted features of claims 1 and 21.

Schwendeman appears to teach formation of a mixed polymer that includes one or more functional groups capable of forming covalent linkages with a bioactive molecule. For example, Schwendeman states:

The SAFP further comprises functional groups which are covalently bonded to the backbone of the SAFP or pendant groups which are attached to the hydrophilic region of the SAFP backbone. The functional groups encompass conjugatable groups such as for example amines, hydroxyls, carbonyls, thiols, and carboxylic acids for covalently bonding of other bioactive molecules to the surface of the particle. The linkages formed following conjugation of the bioactive molecules to the conjugatable groups include amides, esters, and thioethers.

(Schwendeman, col. 3, lines 33-40)

Contrary to the teachings of Schwendeman, Applicant’s claims are directed to encapsulating a biopharmaceutical compound by using ionic interactions between the compound and the particle. As such, Applicant submits that the combination of Supersaxo and Schwendeman does not appear to teach or suggest all of the features of Applicant’s claims.

E. The Claims Are Patentable Over Supersaxo In View Of Mady Pursuant to 35 U.S.C. §103(a)

The Examiner rejected claims 1, 10, 11, 21, 29-30, 32 and 33 under 35 U.S.C. § 103(a) as obvious over Supersaxo in view of Mady et al., “Studying the effect of surfactant on Eudragit microspheres prepared by solvent evaporation.” (hereinafter “Mady”). Applicant respectfully disagrees that the claims are unpatentable over Supersaxo in view of Mady.

The Office Action states that, “Supersaxo et al. discloses a controlled release pharmaceutical composition comprising a physiologically active agent dispersed in preformed porous polymeric microparticles.” (Office Action, page 4) The Examiner concedes that “Supersaxo does not disclose the microparticles having accessible ionic functional groups.”

Claims 1 and 21 include a combination of features including, but not limited to, the features of “preparing biodegradable porous microspheres comprising cationic functional groups.” Applicant submits that the cited art does not appear to teach or suggest at least the quoted features of claims 1 and 21. Applicant submits that biodegradable porous microspheres are microspheres that will degrade over time in the body. Supersaxo appears to teach the use of biodegradable polymers. Mady, however, does not appear to teach or suggest the use of biodegradable polymers. Specifically, Mady is directed to the formation of Eudragit polymers which are polyacrylate polymers. For at least the same reasons recited above with respect to the Rembaum reference, Applicant submits that the combination of Supersaxo and Mady does not appear to teach or suggest all of the features of Applicant’s claims.

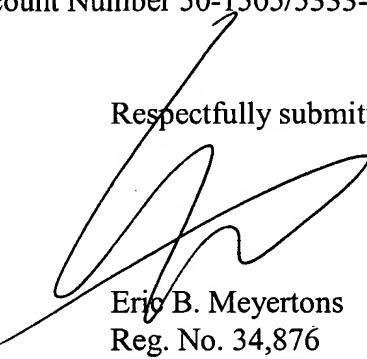
Additionally, Mady’s use of a surfactant is for a different purpose than Applicant’s claimed use. Mady appears to teach that the surfactant is not intended to be incorporated into the microsphere, rather it is intended to inhibit aggregation during the preparation of the microspheres. Additionally, Applicant notes that when preparing microspheres using a solvent evaporation method the added surfactant is only added to the aqueous phase. Further, the article describes the use of centrimide, a cationic surfactant, and DOSS an anionic surfactant, both of which were used in the encapsulation of an acidic medicine, ibuprofen. When the cationic surfactant, centrimide, was increased to 1.5%, reduction of the encapsulation ratio of the medicine was observed.

F. Additional Comments

Applicant submits that all claims are in condition for allowance. Favorable reconsideration is respectfully requested.

Applicant hereby requests a three-month extension of time. A fee authorization for a three-month extension of time is included. If any additional extension of time is required, Applicant hereby requests the appropriate extension of time. If any additional fees are required or if any fees have been overpaid, please appropriately charge or credit those fees to Meyertons, Hood, Kivlin, Kowert & Goetzel, P.C. Deposit Account Number 50-1505/5333-02600/EBM.

Respectfully submitted,



Eric B. Meyertons
Reg. No. 34,876

Attorney for Applicants

MEYERTONS, HOOD, KIVLIN, KOWERT & GOETZEL, P.C.
P.O. Box 398
Austin, TX 78767-0398
(512) 853-8800 (voice)
(512) 853-8801 (facsimile)

Date: 4/5/05